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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,168	08/26/2003	Volker Albrecht	BJA319A	4452

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/648,168	ALBRECHT ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,8,10,11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6, 8, 10-11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 8-4-06 is acknowledged.

Claims included in the prosecution are 1-2, 6, 8, 10-11 and 13.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-2 and 6, 8, 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Madden (5,389,378).

Madden discloses liposomal formulations containing porphyrins. The phospholipids included dipalmitoylphosphatidylcholine and the liposomes are either in a suspended form or as a lyophilized powder and contain mannitol or glucose (abstract, col. 7, line 8 through col. 9, line 62, Examples and claims). The amounts of the sugars (expressed in millimolar quantities) and the amounts of porphyrins (which are expressed in microgram quantities) as evident from the examples fall within the broad ranges claimed.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that a key point in the referenced abstract is that after reciting a general description of possible lipid components and benzoporphyrin, in line 9 it states "In an additional aspect ---sized liposomes are described which are storage

stable" and that this implies that to be storage stable a liposomal formulation may require restrictions or additions beyond the basic components. This argument is not persuasive since stability, which the abstract describes, is the stability during sterilization and during lyophilization. That the liposomes can be safely dehydrated is evident from col. 7, line 43 et seq. applicant further argues that the present invention relies on synthetic phospholipids like DPPC and DPPG to the exclusion of naturally-derived phospholipids which include the preferred egg phosphatidylcholine, EPC of Madden. This argument is not found to be persuasive since Madden's example 1 on col. 12 clearly shows the preparation of DMPC liposomes. DMPC is a synthetic lipid. Madden also discloses synthetic phospholipids such as DPPC and DPPG on col. 8. Applicant's arguments that Madden already states that sugars are known to be needed to permit freeze-drying to dehydration prior to storage. This argument is not persuasive since instant claims recite the presence of a monosaccharide just as in Madden. Applicant's arguments that Madden states that sucrose and trehalose are most effective are not persuasive since Madden teaches even glucose on col. 9. The rejection is maintained.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 6, 8, 10-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al in view of Madden both cited and discussed above.

Desai et al disclose liposomal compositions containing hematoporphyrin, protoporphyrin, deuteroporphyrin and other porphyrins. Dipalmitoylphosphatidylcholine is the preferred phospholipid in making the liposomes. The liposomes are either in suspension form or as a lyophilized powder and contain disaccharides or polysaccharides. The compositions further contain ascorbyl palmitate. The concentration of the porphyrins ranges from 0.1 % up to 0.5 % (abstract, col. 3, lines 43-52, col. 7, line 3 through col. 8, line 52 and claims).

What is lacking in DESAI et al is the use of monosaccharides such as glucose or polyols such as mannitol. The use of these sugars would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since MADDEN teaches that dehydration of the liposomes can be done with a variety of sugars including those taught by DESAI et al and monosaccharides such as glucose and polyols such as mannitol.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Desai et al disclose numerous liposomal compositions primarily for hydro-mono benzoporphyrins and a wide range of phospholipids and as in Madden, there is a preference for egg phosphatidyl derivative EPG, a naturally derived phospholipid. These arguments are not persuasive since on col. 5, line 24, Desai et al clearly states that one or more phospholipids could be used and on the same column, line 60 et seq., list several synthetic phospholipids, which

include, DPPC, DSPC. Furthermore, in all the examples on columns 9 and 10, Desai et al use a synthetic phospholipid although along with a natural phospholipid. One of ordinary skill in the art would have been motivated to use only synthetic phospholipid based on Desai et al's statement, 'one or more phospholipid' and also because Madden shows the use of liposomes using only synthetic phospholipids. Applicant has not shown any unexpected results obtained by using a combination of phospholipids taught by Desai et al. Applicant argues that despite 378 teach the use of variety of sugars including monosaccharides, both cited references reject the use of monosaccharides in porphyrin derivative liposome formulations and instead both reference indicate that certain desirable characteristics either would be hindered or precluded with the use of monosaccharides in a porphyrin –liposome formulation. This argument is not found to be persuasive since applicant does not state where in the references such is taught. Applicant's arguments that neither reference has given any indication that monosaccharides will protect any phospholipid liposomal formulations containing a non-polar photosensitizer during freeze-drying and reconstitution. This argument is not persuasive since Madden on col. 9, lines 12-15 only states that in general, disaccharide sugars have been found to work better than monosaccharide sugars; this statement does not mean that monosaccharides do not work at all. Applicant's arguments regarding to percentage of monosaccharides and sizes of the particles are not persuasive since the independent claims do not recite any percentages and just a finding that they function well does not impart patentability to the claims.

5. Claims 1-2, 6, 8, 10-11 and 13 are rejected under 35 U.S.C. 103(a) as being

unpatentable over GB 2146525 also cited and discussed above, in view of MADDEN cited and discussed above.

GB as pointed out above discloses liposomal formulations containing hematoporphyrin, protoporphyrin, deuteroporphyrin and other porphyrins. The liposomes contain an additional anti-cancer agent (abstract, pages 5-6 and claims).

What are lacking in GB are the teachings of lyophilizing the liposomes in the presence of sugars or polyols. Although GB teaches the use of phosphatidylcholine, it does not specifically teach that the phosphatidylcholine be dipalmitoylphosphatidylcholine.

Madden as discussed above, discloses liposomal formulations containing porphyrins. The phospholipids included dipalmitoylphosphatidylcholine and the liposomes are either in a suspended form or as a lyophilized powder and contain mannitol or glucose (abstract, col. 7, line 8 through col. 9, line 62, Examples and claims). The amounts of the sugars (expressed in millimolar quantities) and the amounts of porphyrins (which are expressed in microgram quantities) as evident from the examples fall within the broad ranges claimed. According to Madden, the dehydrated liposomes, dehydrated in presence of protective sugars are storage stable and can be stored for extended periods of time (col. 9, lines 31-62).

It would have been obvious to one of ordinary skill in the art to used dipalmitoylphosphatidylcholine as the specific phosphatidylcholine in the liposomes of GB with a reasonable expectation of success since Madden teaches its routine in the liposomes containing porphyrins. It would have been obvious to one of ordinary skill in

the art to dehydrate (freeze-dry) the liposomes of GB in the presence of protective sugars such as glucose or mannitol since dehydrated liposomes can be are storage stable and can be stored for extended periods of time as taught by Madden.

Applicant's arguments have been fully considered, but are not found to be persuasive. Arguments regarding Madden have been addressed above. Applicant while agreeing that the references 378, 666, and GB all mention components identified in claim 1 and some subsequent claims, the point that seemed to be missing is that to achieve stable vesicles which can withstand freeze-drying and reconstitution using monosaccharides. These arguments as pertaining to Madden and Desai have been addressed above. Furthermore, applicant has not shown that the prior art liposomes including those in GB are not stable to freeze-drying. The rejection is maintained.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ S Kishore

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK